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10/538,442	09/11/2006	Jean Pierre Gayral	GENOM.061NP	3808

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EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

NOTIFICATION DATE	DELIVERY MODE
10/22/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/538,442	GAYRAL ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *1-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-46* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 8/8/2007 is acknowledged and has been entered. Claims 1, 4, 6, 15, 16, 30, 32, and 46 have been amended. Claims 1-46 are pending. Claims 1-14 have been withdrawn from consideration as being drawn to a non-elected invention. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The objection to the claims are withdrawn in view of Applicant's amendment. The claim rejection under 35 USC 112 second paragraph is withdrawn in part based on Applicant's amendment. The prior art rejection under 35 USC 102(b) as being anticipated by Ke et al is maintained and discussed below. The prior art rejection under 35 USC 102(b) as being anticipated by Saldanha is maintained and discussed below. The prior art rejection under 35 USC 102(a) as being anticipated by Picard and Bergeron. The prior art rejection under 35 USC 103(A) as being unpatentable over Ke et al in view of Kuska et al is maintained and discussed below.

35 USC 112 second paragraph

4. Once again, claims 28 is confusing at " a 10 sample of clinical, environmental or alimentary origin" because it unclear what is meant by "a 10 sample". Specifically, it is unclear if Applicant is suggesting that the sample comprise a total of 10 test samples to be analyzed that are from each of a clinical environmental or alimentary origin or if applicant is suggesting a desired name, property or characteristic for the test sample or something completely different. Clarification is required.

Response to Arguments

5. Applicant states that the claims have been amended to delete the term "10" from the claim. However, it is noted that the claims 28 has not been amended in any manner. The claim recites "a 10 sample" which is confusing in the context of the claim language. Accordingly, this rejection is maintained.

Claim Rejections - 35 USC § 102(b)

6. Once again, claims 15, 16, 18-21, 23-29, 31-32, 34-37, 39-45 are rejected under 35 USC 102(b) as being anticipated by Ke et al (Clinical Chemistry, vol. 46, no. 3, pages 324-331, 2000). Regarding claims 15 and 32, Ke et al teach a method comprising providing a reagent comprising a cell comprising a bacterial cells comprising at least one nucleic acid sequence serving as an internal control target sample preparation; adding said reagent into said test sample; submitting said released, nucleic acid to amplification or detection (page 325, "construction of the internal control" and "PCR amplification"; see also "Table 3").

Regarding claim 16, Ke et al teach a method as defined in claim 15, further comprising comparing the amplification and/or detection performed in iv) to the amplification and/or detection performed with control reaction to evaluate the efficiency of sample preparation ("PCR amplification" and "Specificity and Sensitivity tests").

Regarding claims 18 and 34, Ke et al teach the method of claims 15 or 16, wherein said cells is bacteria (Table 1).

Regarding the claims 19 and 35, Ke et al teach the method of claims 15 or 16, wherein said cells is *E. coli* (page 325, col. 2, "construction of the internal control" and Table 1).

Regarding claims 20 and 36, Ke et al teach the method of claims 15 or 16, wherein said cells are bacterial spores (Table 1).

Regarding claims 21, and 37; Ke et al teach the method of claims 15 or 16, wherein said cells are bacterial spores such as Bacillus anthracis (page 326, Table 1).

Regarding claims 23 and 39, Ke et al teach the method of claims 15 or 16, wherein said IC target nucleic acid sequence is on a cloning vector (page 325, col. 2, "construction of the internal control").

Regarding claims 24 and 40, Ke et al teach the method of claims 23 or 39, wherein said IC target nucleic acid sequence is on a plasmid vector (page 325, col. 2, "construction of the internal control").

Regarding claims 25 and 41, Ke et al teach the method of claim 15, wherein said nucleic acid amplification method is PCR ("PCR amplification"; see also "Table 3").

Regarding claims 26 and 42, Ke et al teach the method of claim 15, wherein said IC nucleic acid sequence is a nucleic acid sequence of clinical origin and of human origin (page 325, col. 1, section entitled "Microorganisms" and "DNA Isolation").

Regarding claim 27 and 43; Ke et al teach the method of claim 15, wherein the IC target nucleic acid sequence is a nucleic acid sequence of microbial origin (see page 325, section entitled "Microorganisms" and "DNA Isolation").

Note* For the purpose of application of prior art, the claimed limitation "a 10 sample" is being interpreted by the Examiner as a minimum amount of samples to be analyzed by the method. Regarding claims 28 and 44, Ke et

al teach the method of claim 15, wherein the test sample comprises over 10 samples of clinical origin (page 327, "clinical specimens and GBS-selective culture and PCR").

Regarding claims 29 and 45, Ke et al teach wherein the test sample comprises a vaginal/anal swab (page 327, "clinical specimens and GBS-selective culture and PCR" and Table 1).

Regarding claim 31, Ke et al teach the method of claim 15, wherein said reagent may be a bacterial spore which allows one to determine the efficiency of the sample preparation (see Table 1). Therefore, Ke et al meet the limitations of the claims recited above.

Response to Arguments

7. Applicant's traverses the rejection on the grounds that Ke et al do not add a reagent comprising cells or organelles to a test sample. Applicant states that Ke et al do not process the test sample with added reagents release, purify and/or concentrate nucleic acids of both the test sample and added reagents, and Ke et al do not submit released, purified and/or concentrated nucleic acids from the sample preparation step to amplification and/or detection for the amplification of both said IC and test sample nucleic acids. Applicant states that Ke do not provides a mean to verify the efficiency of sample preparation.

All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In response to applicant's arguments that the claims do not teach adding a reagent comprising cells or organelles to a test sample, this argument is not found persuasive because Ke et al expressly teach wherein a reagent comprising an internal control is added to the target sample, said target sample being Group B streptococci and vaginal and anal flora (see page 325, 327 and especially Table 3, which teaches that the internal control was coamplified with sample in conventional PCR and Figure 1 with legend).

In regards to Applicant's arguments that Ke et al do not teach the steps of releasing or purifying or concentrating the sample and further analysis, it is noted that Ke expressly teach releasing the target nucleic acid and performing steps of real-time fluorescence monitoring to detection as broadly claimed in the instant invention (See "Discussion", especially page 330). The Examiner maintains that Applicant's arguments are not sufficient to overcome the prior art rejection. Accordingly, this rejection is maintained.

Claim Rejections - 35 USC § 102

8. Claims 15-17, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Saldanha, John (Journal of Clinical Virology, vol. 20, pages 7-13, January 2001). Regarding claims 15 and 32, Saldanha teaches a method comprising providing a reagent comprising a cell comprising a viral particle comprising at least one nucleic acid sequence serving as an internal control target sample preparation; adding said reagent into said test sample; submitting said released, nucleic acid to amplification or detection to determine efficiency of the sample preparation (abstract and page 11-12, "Quality control of NAT assays").

Regarding claim 16, Saldanha teaches further comprising comparing the amplification and/or detection performed in iv) to the amplification and/or detection performed with control reaction to evaluate the efficiency of sample preparation (page 8-10, sections 2 and 3 and Tables 1-3).

Regarding claim 17 and 33, Saldanha teaches wherein said sample preparation procedures comprise concentrating said cells comprising viral particles prior to lysis (abstract and section entitled "development of working reagents"). Therefore Saldanha meets the limitations of the claims recited above.

Response to Arguments

9. Applicant traverse the rejection on the grounds that Saldanha does not mention the use of cells comprising viral particles, or any other of the reagents recited in Applicant's claim as a reagent for an internal control. Applicant asserts that the "lyophilized preparation" as taught by Saldanha are not cells, organelles, parasites, cells comprising organelles, cells comprising viral particles, cells comprising parasites, cells comprising bacterial cells, or any combination thereof".

These arguments are not found persuasive. Applicant argues that the prior art "lyophilized preparation" does not meet the limitation of " a cell" or "organelle" or "viral particle". However, Applicant fails to properly interpret this limitation. The Federal Circuit discussed claim interpretation by the PTO in *In re Morris*, where the Federal Circuit noted "[A]s an initial matter, the PTO applies to the verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 44 USPQ2d 1023, 1029 (Fed. Cir. 1997). The decision of the court in *In re Bigio*, 72 USPQ2d 1209 (Fed. Cir. 2004) strongly supports the breadth of interpretation. That court noted "[T]his court counsels the PTO to avoid the temptation to limit broad claim terms solely on the basis of specification passages." In concert with *Morris* and *Bigio* is the decision in *In re American Academy of Science Tech Center*, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004), where the Federal Circuit noted "We have cautioned against reading limitations into a claim from the preferred embodiment described in the specification, even if it is the only embodiment described, absent clear disclaimer in the specification."

In this case, the specification defines "a cell" at page 20" as broadly covering any eukaryote or prokaryote cell, including for example plant cells, mammalian cells, parasites, unicellular organisms, yeasts, fungi, and bacterial cells. The specification teaches at page 20 that the terminology "organelle", which is well known in the art is meant to cover any cellular organelle from cells. The specification does not provide any

limiting definition for the term "viral particles". The art defines a "lyophilized preparation" as a tissue, blood, serum, or other biological substances; dried in a freezed state. Thus, a lyophilized preparation encompasses cells and/or organelles. Further, Saldanha teaches that the lyophilized preparation is from a blood sample comprising hepatitis A virus, hepatitis C virus and human immunodeficiency virus, which not only comprise cells, but also viral particles. Therefore, given the broad definition of the terms in the specification, lack of a limiting definition for a viral particle, and the broadest reasonable interpretation of the claims, the prior art of Saldanha is within the scope of the term "cell" and "viral particle" as required by the specification and claims. Applicant's arguments are not sufficient to overcome the prior art rejections.

Claim Rejections - 35 USC § 102

10. Once again, claims 15-21, 30, 32-34, 36, 37, 46 are rejected under 35 U.S.C. 102(a) as being anticipated by Picard and Bergeron (Drug Discovery Today, vol. 7, Issue 2, pages 1092-1101, November 2002). Regarding claims 15, 16 and 32, Picard and Bergeron teach a method comprising providing a reagent comprising a cell comprising a bacterial cells comprising at least one nucleic acid sequence serving as an internal control target sample preparation; adding said reagent into said test sample; submitting said released, nucleic acid to amplification or detection and further comparing the amplification and/or detection with control reactions to evaluate the efficiency of the sample preparation (see sections 2.2 and 2.5-2.5.3.).

Regarding claims 17 and 33, Picard and Bergeron teach wherein said sample preparation comprises purifying the cells prior to lysis (section 2.2).

Regarding claims 18 and 34, Picard and Bergeron teach wherein said cell is selected from bacteria (section 2.2).

Regarding claim 20, 21, 36 and 37, Picard and Bergeron teach wherein said cell are bacillus spores (section 2.2).

Regarding claim 30 and 46, Picard and Bergeron teach wherein the sample preparation comprises concentrating and purifying cells or viral particles lysis of cells, nucleic acid extraction, inactivation, elimination or neutralization of Nat inhibitors and or nucleic acid concentration or purification (see section 2.2 and 2.5 to 2.5.2). Therefore, Picard and Bergeron meet the limitations of the claims as recited above.

Response to Arguments

11. Applicant traverses the rejections on the grounds that Picard et al do not teach adding a reagent that is a cell or organelle harboring internal control sequences to a test sample, and isolating purifying and/or concentrating the nucleic acids from the test with the added reagents. Applicant states that Picard et al teach that the internal controls are integrated into the NAT assay and are designed to verify the efficiency of each amplification and or detection reaction. Applicant states that Picard is silent regarding the addition of a reagent that comprise cells and organelles to a test sample followed by a step of releasing, purifying and or concentrating the nucleic acids from the test sample and added reagents.

In response to Applicant, it is noted that Picard meets this limitation because Picard teaches that the internal controls are integrated into the NAT assay (2.5.2). In order to be integrated into the NAT assay, the internal controls must be added to sample comprising the target samples (cells). Picard provides examples of a NAT assay which comprises "a cartridge which is a closed microfluidic system containing all necessary reagents, components and chambers for microbial cell lysis and test sample preparation for NAT (page 5). This suggests the reagent coming into contact with the target sample (cells) as required by the claim. Picard also teaches wherein subsequent PCR amplification and fluorescence based detection (page 5). Applicant's arguments are not sufficient to overcome the prior art rejections.

Claim Rejections - 35 USC § 103

12. Claims 22 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ke et al as previously applied above in view of Kuske et al (Applied and Environmental Microbiology, July 1998, vol. 64, no. 7, pages 2463-2472). Regarding claims 22 and 38, Ke et al teach a method for verifying the efficiency of sample preparation as previously discussed above, wherein said method comprises providing a reagent comprising a cell wherein said cell

may be bacterial spores and wherein said cell comprises at least one nucleic acid serving as an internal control target sample preparation.

Ke et al differs from the instant invention in that the reference does not teach wherein the bacterial spores are *Bacillus globigii* spores.

Kuske et al teach a method for determining the efficiencies of a sample preparation for PCR amplification and detection wherein said sample is an environmental sample comprising cells of Bacillus globigii endospores (see Material and Methods and page 2471, last paragraph of col. 1 bridging first two paragraphs of col. II). Kuske et al teach that there is a need for detecting microbial cells and spores in soil or environmental samples. Kuske et al teaches that while the art provides methods for extracting DNA from microbial spores in soil, the spore forming bacterial DNA is often severely sheared and does not provide for the highest PCR detection sensitivity (page 2463, col. 2). Kuske additionally teaches that environmental samples, which may comprise spore-forming bacterial cells, are often difficult to obtain, may be present in very low concentrations and/or partially degraded or compromised by chemical treatment (page 2471). Therefore, in view of the foregoing one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the method of Ke et al to encompass other spore forming bacterial microbes such as *B. Globigii* et al for the benefit of increases sensitivity of PCR detection of environmental samples as suggested by Kuske. One of ordinary skill in the art would have been motivated to do so based on the need in the art as taught by Kuske for detecting microbial DNA from environmental samples, such as soil.

Response to Arguments

13. Applicant traverses the rejection on the same grounds as those discussed above for Ke et al. Applicant states that Ke et al do not teach the step of adding a reagent comprising cells or organelles to a test sample and the secondary reference of Kruske et al do not correct the deficiencies of Ke et al.

This argument is not found persuasive for the reasons discussed above at # 7. The examiner maintains that the combination of Ke et al in view of Kruske et al meet the limitations of the claims.

New Grounds of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Objections

14. Claim 16 is objected to because of the following informalities: The word "regent" is misspelled in the context of the claims. It is suggested amending the claim to recite --reagent--. Appropriate correction is required.

Conclusion

1. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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